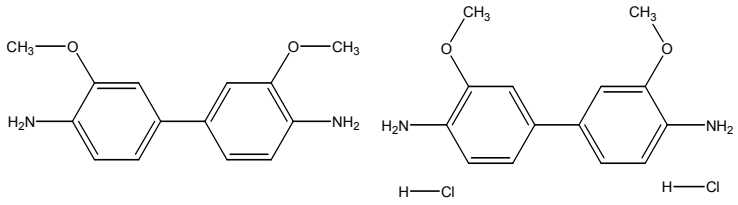
3,3'-DIMETHOXYBENZIDINE AND 3,3'-DIMETHOXYBENZIDINE DIHYDROCHLORIDE

CAS Nos. 119-90-4 and 20325-40-0

First Listed in the *Third Annual Report on Carcinogens*



3,3'-Dimethoxybenzidine 3,3'-Dimethoxybenzidine dihydrochloride

CARCINOGENICITY

3,3'-Dimethoxybenzidine is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC V.4, 1974; IARC S.4, 1982). When administered by gavage, 3,3'-dimethoxybenzidine induced tumors at various sites including Zymbal gland tumors, intestinal carcinomas, skin carcinomas, and urinary bladder papillomas in rats of both sexes. When administered in the diet, 3,3'-dimethoxybenzidine increased the incidence of forestomach papillomas. When administered in the drinking water, 3,3'-dimethoxybenzidine dihydrochloride increased the incidence of Zymbal gland adenomas and carcinomas, liver neoplastic nodules or hepatocellular carcinomas, large intestine adenomatous polyps or adenocarcinomas, and squamous cell papillomas or carcinomas of the oral cavity in rats of both sexes; preputial gland carcinomas, basal cell adenomas and carcinomas of the skin, adenocarcinomas of the small intestine, and mesotheliomas in male rats; and clitoral gland adenomas and carcinomas, basal cell adenomas or carcinomas of the skin, mammary gland adenocarcinomas, and uterus/cervix adenomas or carcinomas in female rats (NTP 372, 1990).

There is inadequate evidence for the carcinogenicity of 3,3'-dimethoxybenzidine in humans. No epidemiological data on the occurrence of cancer in workers exposed to 3,3'-dimethoxybenzidine alone appear in the literature. Most of the workers exposed to this substance were also exposed to related amines, such as benzidine, which are strongly associated with urinary bladder cancer in humans (see Benzidine, Section III.A) (IARC, V.4, 1974; IARC S.4, 1982; IARC S.7, 1987).

PROPERTIES

3,3'-Dimethoxybenzidine, also known as *o*-dianisidine, occurs as colorless crystals which turn violet upon standing. It is virtually insoluble in water and probably soluble in most organic solvents (e.g., ethanol, ether, acetone, benzene, and chloroform). 3,3'-Dimethoxybenzidine is available commercially as the free base (technical and 99% grades) and as its dihydrochloride salt. When heated to decomposition, 3,3'-dimethoxybenzidine emits toxic fumes of nitrogen oxides (NO_x).

USE

3,3'-Dimethoxybenzidine is used principally as a chemical intermediate for the production of azo dyes. The Society of Dyers and Colourists reported its use as an intermediate in the production of 89 dyes in 1971. Among the dyes listed were Direct Blue 218, Pigment Orange 16, Direct Blue 1, Direct Blue 15, Direct Blue 8, Direct Blue 76, and Direct Blue 98. About 30% of the 3,3'-dimethoxybenzidine consumed is used as a chemical intermediate to produce *o*-dianisidine diisocyanate for use in adhesive systems and as a component of polyurethane elastomers and resins. 3,3'-Dimethoxybenzidine is used as a dye for leather, paper, plastics, rubber, and textiles, and a reagent to detect metals, thiocyanates, and nitrites (IARC V.4, 1974).

PRODUCTION

The 1998 *Chemical Buyers Directory* and *Chemcyclopedia 98* did not list any suppliers of 3,3'-dimethoxybenzidine (Tilton, 1997; Rodnan, 1997), and the 1997 *Directory of Chemical Producers* identified no producers of the compound (SRIa, 1997). Chmfinder (1998) listed one domestic company that supplies the chemical. U.S. imports of 3,3'-dimethoxybenzidine were reported by the USITC to be 106,000 lb and imports of 3,3'-dimethoxybenzidine and its dihydrochloride were reported to be 655,000 lb in 1983 (USITCa, 1984). The 1979 TSCA Inventory identified two companies producing an unspecified amount of 3,3'-dimethoxybenzidine and six companies importing 55,500 lb in 1977. The CBI Aggregate was less than 1 million lb (TSCA 1979). U.S. imports of 3,3'-dimethoxybenzidine through the principal custom districts were reported to be 273,000 lb in 1971. Data on domestic production of 3,3'-dimethoxybenzidine were last reported in 1967, when five companies produced 368,000 lb. 3,3'-dimethoxybenzidine has been produced commercially for at least 50 years (IARC V.4, 1974).

EXPOSURE

The primary routes of potential human exposure to 3,3'-dimethoxybenzidine are inhalation and dermal contact. Exposure to 3,3'-dimethoxybenzidine can occur during its use as a chemical intermediate in the production of azo dyes, *o*-dianisidine diisocyanate formulations, textile processing, and packaging processes. Workers potentially exposed to the chemical include dye makers and *o*-dianisidine diisocyanate production workers. However, present dye production processes for 3,3'-dimethoxybenzidine and its dye derivatives are generally closed systems with minimal risk to workers. The National Occupational Hazard Survey, conducted by NIOSH from 1972 to 1974, estimated that 204 workers were possibly exposed to 3,3'-dimethoxybenzidine in the workplace (NIOSH, 1976). The National Occupational Exposure Survey (1981-1983) estimated that 2,482 workers were potentially exposed to the compound (NIOSH, 1984). Potential human exposure may occur as a result of the presence of trace contaminants in end products that are formulated with 3,3'-dimethoxybenzidine (e.g., azo dyes, pigments, adhesives, resins, and polyurethane elastomers). CPSC is concerned that these dyes and pigments contain residual levels or trace impurities of 3,3'-dimethoxybenzidine in the ppm range and that traces may be present in the final consumer products. Presently, no data are available on the actual quantities in the final consumer products. A dermal penetration study in rabbits indicated that a 3,3'-dimethoxybenzidine-based dye was not absorbed in significant amounts.

The Toxic Chemical Release Inventory (EPA) reported an environmental release from one facility that produced, processed, or otherwise used 3,3'-dimethoxybenzidine dihydrochloride in the United States in 1996. The facility, located in Spartanburg, South Carolina, reporting under

the industrial classification for manufacture of industrial organic chemicals not elsewhere classified (SIC Code 2869) and cyclic crudes and intermediates (SIC Code 2865), released a total of 10 lb to air (TRI96, 1998).

REGULATIONS

In late 1980, CPSC started collecting data to propose a ban on the use of 3,3'-dimethoxybenzidine-based dyes in mass-merchandised consumer dye products; however, the use of benzidine congener dyes in consumer household dyeing products and in commercial textile applications has been decreased voluntarily. Artists and crafts people have been alerted to potential hazards from inhaling powders of dyes based on 3,3'-dimethoxybenzidine. EPA regulates 3,3'-dimethoxybenzidine under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), Resource Conservation and Recovery Act (RCRA), and Superfund Amendments and Reauthorization Act (SARA). An adjustment of the statutory reportable quantity (RQ) from 1 lb to 100 lb has been established for this chemical under CERCLA. RCRA regulates 3,3'-dimethoxybenzidine as a hazardous constituent of waste. EPA has included 3,3'-dimethoxybenzidine on a list of priority hazard substances under SARA. OSHA regulates 3,3'-dimethoxybenzidine and its dihydrochloride salt under the Hazard Communication Standard and as chemical hazards in laboratories. Regulations are summarized in Volume II, Table B-49.